Attorney Docket No.: IMARX1360-2

In re Application of: Evan C. Unger

Application No.: 10/622,027

Filed: July 16, 2003

Page 2 of 16

IN THE CLAIMS

Please amend claims 1-4, 6-10, 13-15, 20, 23-25, 41, 42, 44, and 45 as shown below. Please cancel claims 39, 40, and 43 without prejudice. Please add new claims 46-53. The following listing of claims replaces all prior listings.

- 1. (Currently amended) A therapeutic composition comprising a solid porous matrix comprising a surfactant and a therapeutic, wherein the matrix contains a gas and/or a gas precursor entrapped therein and the gas and/or the gas precursor is selected from a group consisting of a perfluorocarbon, a perfluoroether, sulfur hexafluoride, and combinations thereof.
- 2. (Currently amended) The therapeutic composition according to claim 1, wherein said composition is in a physical state selected from a dried state and a liquid state.
- 3. (Currently amended) The therapeutic composition according to claim 2, wherein said composition is in a liquid state further rehydrated with an aqueous solution.
- 4. (Currently amended) The therapeutic composition according to claim 3, wherein the composition said liquid state further comprises a resuspending medium.
 - 5. (Canceled).
- 6. (Currently amended) The therapeutic composition according to claim 4, wherein said resuspending medium is selected from the group consisting of water, buffer, physiological saline, and normal saline.
- 7. (Currently amended) The therapeutic composition according to claim 1, further comprising an additive selected from the group consisting of polyethylene glycol, sucrose, glucose, fructose, mannose, trehalose glycerol, propylene glycol and sodium chloride.

Attorney Docket No.: IMARX1360-2

In re Application of: Evan C. Unger

Application No.: 10/622,027

Filed: July 16, 2003

Page 3 of 16

8. (Currently amended) The therapeutic composition according to claim 7, wherein said additive is selected from the group consisting of polyethylene glycol and sucrose.

- 9. (Currently amended) The therapeutic composition according to claim 8, wherein said additive is polyethylene glycol.
- 10. (Currently amended) The therapeutic composition according to claim 9, wherein said polyethylene glycol is PEG-400.
- 11. (Withdrawn) The therapeutic composition according to claim 1 wherein said polysorbate surfactant is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 60 and polysorbate 80.
- 12. (Withdrawn) The therapeutic composition according to claim 9 wherein said polysorbate surfactant is polysorbate 80.
- 13. (Currently amended) The therapeutic composition according to claim 1, wherein said therapeutic is selected from the group consisting of antineoplastic agents, blood products, biological response modifiers, antifungal agents, P-lactam antibiotics, hormones, vitamins, peptides, enzymes, antiallergic agents, anticoagulation agents, circulatory drugs, antituberculars, antivirals, antianginals, antibiotics, antiinflammatories, antiprotozoans, antirheumatics, narcotics, cardiac glycosides, neuromuscular blockers, sedatives, anesthetics, radioactive particles, monoclonal antibodies, and genetic material.
- 14. (Currently amended) The therapeutic composition according to claim 13, wherein said antineoplastic agent is selected from the group consisting of platinum compounds, adriamycin, mitomycin, ansamitocin, bleomycin, cytosine arabinoside, arabinosyl adenine, mercaptopolylysine, vincristine, busulfan, chlorambucil, melphalan, mercaptopurine, mitotane, procarbazine hydrochloride, dactinomycin, daunorubicin hydrochloride, doxorubicin hydrochloride, taxol, mitomycin, plicamycin,

Attorney Docket No.: IMARX1360-2

In re Application of: Evan C. Unger

Application No.: 10/622,027

Filed: July 16, 2003

Page 4 of 16

aminoglutethimide, estramustine phosphate sodium, flutamide, leuprolide acetate, megestrol acetate, tamoxifen citrate, testolactone, trilostane, amsacrine, asparaginase, etoposide, interferon, teniposide, vinblastine sulfate, vincristine sulfate, bleomycin, methotrexate, and carzelesin.

- 15. (Currently amended) The therapeutic composition according to claim 14, wherein said antineoplastic agent is taxol.
- 16. (Withdrawn) The therapeutic composition according to claim 13, wherein said therapeutic is selected from the group consisting of ketoconazole, nystatin, griseofulvin, flucytosine, miconazole, amphotericin B, ricin, and |3-lactam antibiotics.
- 17. (Withdrawn) The therapeutic composition according to claim 16, wherein said therapeutic is amphotericin B.
- 18. (Withdrawn) The therapeutic composition according to claim 17 wherein said solid porous matrix is between about 100 nm and 2 microns in diameter.
- 19. (Previously presented) A solid porous matrix comprising a surfactant in combination with a therapeutic prepared by combining a solvent, a surfactant, and a therapeutic to form an emulsion of said surfactant and said therapeutic; and processing said emulsion by controlled drying or controlled agitation and controlled drying, to form said solid porous matrix.
- 20. (Currently amended) The solid porous matrix according to claim 19, wherein said solvent is evaporated during said processing.
 - 21-22. (Canceled).
- 23. (Currently amended) The solid porous matrix according to claim 19, wherein said therapeutic is selected from the group consisting of antineoplastic agents, blood products, biological response modifiers, antifungal agents, |3-lactam antibiotics,

Attorney Docket No.: IMARX1360-2

In re Application of: Evan C. Unger

Application No.: 10/622,027

Filed: July 16, 2003

Page 5 of 16

hormones, vitamins, peptides, enzymes, antiallergic agents, anticoagulation agents, circulatory drugs, antituberculars, antivirals, antianginals, antibiotics, antiinflammatories, antiprotozoans, antirheumatics, narcotics, cardiac glycosides, neuromuscular blockers, sedatives, anesthetics, radioactive particles, monoclonal antibodies, and genetic material.

- 24. (Currently amended) The solid porous matrix according to claim 23, wherein said antineoplastic agent is selected from the group consisting of platinum compounds, adriamycin, mitomycin, ansamitocin, bleomycin, cytosine arabinoside, arabinosyl adenine, mercaptopolylysine, vincristine, busulfan, chlorambucil, melphalan, mercaptopurine, mitotane, procarbazine hydrochloride, dactinomycin, daunorubicin hydrochloride, doxorubicin hydrochloride, taxol, mitomycin, plicamycin, aminoglutethimide, estramustine phosphate sodium, flutamide, leuprolide acetate, megestrol acetate, tamoxifen citrate, testolactone, trilostane, amsacrine, asparaginase, etoposide, interferon, teniposide, vinblastine sulfate, vincristine sulfate, bleomycin, methotrexate, and carzelesin.
- 25. (Currently amended) The solid porous matrix according to claim 24, wherein said antineoplastic agent is taxol.
- 26. (Withdrawn) The solid porous matrix according to claim 23, wherein said therapeutic is selected from the group consisting of ketoconazole, nystatin, griseofulvin, flucytosine, miconazole, amphotericin B, ricin, and pMactam antibiotics.
- 27. (Withdrawn) The solid porous matrix according to claim 26 wherein said therapeutic is amphotericin B.
- 28. (Previously presented) The solid porous matrix according to claim 19, having a diameter of between about 100 nm and 2 microns.
- 29. (Withdrawn) A method of preparing a solid porous matrix comprising a surfactant and a therapeutic, said method comprising:

In re Application of:

Evan C. Unger

Attorney Docket No.: IMARX1360-2

Application No.: 10/622,027

Filed: July 16, 2003

Page 6 of 16

a. combining a solvent, a surfactant, and a therapeutic to form an emulsion comprising random aggregates of said surfactant and said therapeutic; and

- b. processing said emulsion by controlled drying, or controlled agitation and controlled drying, to form a solid porous matrix.
- 30. (Withdrawn) The method according to claim 29, wherein said surfactant is selected from the group consisting of nonionic surfactants, oils, lipids, proteins, polypeptides, polysaccharides, sugars, polymers, and acrylates.
- 31. (Withdrawn) The method according to claim 30 wherein said surfactant is a polymer, and is selected from the group consisting of polyglutamic acid, polylysine, polyphosphazene, polyvinylalcohol, polyethyleneglycol, polypropyleneglycol, polylactic acid, poly (e-caprolactone), polylactide co-glycolide, and polyethylene-polypropylene glycol.
- 32. (Withdrawn) The method according to claim 29 wherein said controlled drying is selected from the group consisting of lyophilizing, spray drying, or any combination thereof.
- 33. (Withdrawn) The method according to claim 29 further comprising adding said solid porous matrix to a resuspending medium.
- 34. (Withdrawn) The method according to claim 33 wherein said resuspending medium is selected from the group consisting of an aqueous solution or an organic solution.
- 35. (Withdrawn) The method of claim 34 wherein said resuspending medium comprises an additive selected from the group consisting of polyethylene glycol, sucrose, glucose, fructose, mannose, trehalose glycerol, propylene glycol, and sodium chloride.
- 36. (Withdrawn) The method according to claim 35 wherein said additive is selected from the group consisting of polyethylene glycol and sucrose.

Attorney Docket No.: IMARX1360-2

In re Application of: Evan C. Unger

Application No.: 10/622,027

Filed: July 16, 2003

Page 7 of 16

37. (Withdrawn) The method according to claim 36 wherein said additive is polyethylene glycol.

38. (Withdrawn) The method according to claim 37 wherein said polyethylene glycol is PEG-400.

39-40. (Canceled).

- 41. (Currently amended) The therapeutic composition of claim 1, wherein said surfactant is selected from the group consisting of nonionic surfactants, oils, lipids, proteins, polypeptides, polysaccharides, sugars, polymers, and acrylates.
- 42. (Currently amended) The therapeutic composition of 41, wherein said surfactant is a polymer selected from the group consisting of polyglutamic acid, polylysine, polyphosphazene, polyvinylalcohol, polyethyleneglycol, polypropyleneglycol, polylactic acid, poly(ε-caprolactone), polylactide co-glycolide, and polyethylenepolypropyleneglycol.
 - 43. (Canceled).
- 44. (Currently amended) The solid porous matrix according to claim 20, wherein said surfactant is selected from the group consisting of nonionic surfactants, oils, lipids, proteins, polypeptides, polysaccharides, sugars, polymers, and acrylates.
- 45. (Currently amended) The solid porous matrix according to claim 44, wherein said surfactant is a polymer selected from the group consisting of polyglutamic acid, polylysine, polyphosphazene, polyvinylalcohol, polyethyleneglycol, polypropyleneglycol, polylactic acid, poly(ε-caprolactone), polylactide co-glycolide, and polyethylene-polypropyleneglycol.
- 46. (New) A therapeutic composition comprising a solid porous matrix comprising a surfactant and a therapeutic, wherein the matrix contains a gas and/or a gas

Attorney Docket No.: IMARX1360-2

In re Application of: Evan C. Unger

Application No.: 10/622,027

Filed: July 16, 2003

Page 8 of 16

precursor entrapped therein, and the gas and/or the gas precursor is selected from a group consisting of hexafluoroacetone, isopropyl acetylene, allene, tetrafluoroallene, boron trifluoride, 1,2-butadiene, 2,3-butadiene, 1,3-butadiene, 1,2,3-trichloro-2-fluoro-1,3butadiene, 2-methyl-1,3-butadiene, hexafluoro-1,3-butadiene, butadiene, 1-fluorobutane, 2-methylbutane, perfluorobutane, decafluorobutane, 1-butene, 2-butene, 2-methyl-1butene, 3-methyl-1-butene, perfluoro-1-butene, perfluoro-2-butene, 4-phenyl-3-butene-2one, 2-methyl-1-butene-3-yne, butyl nitrate, 1-butyne, 2-butyne, 2-chloro-1,1,1,4,4,4hexafluorobutyne, 3-methyl-1-butyne, perfluoro-2-butyne, 2-bromobutyraldehyde, carbonyl sulfide, crotononitrile, cyclobutane, methylcyclobutane, octafluorocyclobutane, perfluorocyclobutene, 3-chlorocyclopentene, perfluorocyclopentane, octafluorocyclopentene, cyclopropane, perfluorocyclopropane, 1,2dimethylcyclopropane, 1,1-dimethylcyclopropane-, 1,2-dimethylcyclopropane, ethylcyclo-propane, methylcyclopropane, diacetylene, 3-ethyl-3-methyl diaziridine, 1.1.1-trifluoro-diazoethane, dimethylamine, hexafluorodimethylamine, dimethylethylamine, bis(dimethyl-phosphine)amine, perfluoroethane, perfluoropropane, perfluoropentane, perfluorohexane, perfluoroheptane, perfluorooctane, perfluorononane, perfluorodecane, hexafluoroethane, hexafluoropropylene, octafluoropropane, octafluorocyclopentene, 1,1-dichlorofluoroethane, hexafluoro-2-butyne, octafluoro-2butene, hexafluorobuta-1,3-diene, 2,3-dimethyl-2-norbornane, perfluorodimethylamine, dimethyloxonium chloride, 1,3-dioxolane-2-one, 4-methyl-1,1,1,2-tetrafluoroethane, 1,1,1-trifluoroethane, 1,1,2,2-tetrafluoroethane, 1,1,2-trichloro-1,2,2-t- rifluoroethane, 1,1,2,3,3,3-heptafluoropropane, 1,1,2,2,3,3,3-heptafluoropropane, 1,1-dichloroethane, 1,1-dichloro-ethylene, 1,1-dichloro-1,2-difluoroethylene, 1,1-dichloro-1,2,2,2tetrafluoroethane-, 1,2-difluoroethane, 1-chloro-1,1,2,2,2-pentafluoroethane, 2-chloro-1,1-difluoroethane, 1, 1-dichloro-2-fluoroethane, 1-chloro-1,1,2,2-tetrafluoroethane, 2chloro-1,1-difluoroethane, chloroethane, chloropentafluoroethane, dichlorotrifluoroethane, fluoroethane, nitropenta-fluoroethane, nitrosopentafluoroethane, perfluoroethylamine, ethyl vinyl ether, 1,1-dichloroethane, 1,1-dichloro-1,2difluoroethane, 1,2-difluoroethane, 1,2-difluoroethylene, methane,

Attorney Docket No.: IMARX1360-2

In re Application of: Evan C. Unger

Application No.: 10/622,027

Filed: July 16, 2003

Page 9 of 16

trifluoromethanesulfonylchloride, trifluoromethanesulfenylchloride, (pentafluorothio)trifluoromethane, trifluoromethanesulfonylfluoride, bromodifluoronitrosomethane, bromofluoromethane, bromochlorofluoromethane, bromotrifluoromethane, chlorodifluoronitromethane, chlorodinitromethane, chlorofluoromethane, chlorotrifluoromethane, chlorodifluoromethane, dibromodifluoromethane, dichlorodifluoromethane, dichlorofluoromethane, difluoromethane, difluoroiodomethane, disilanomethane, fluoromethane, perfluoromethane, iodomethane, iodotrifluoromethane, nitrotrifluoromethane, nitrosotrifluoromethane, tetrafluoromethane, trichlorofluoromethane, trifluoromethane, 2-methylbutane, methyl ether, methyl isopropyl ether, methyllactate, methylnitrite, methylsulfide, methyl vinyl ether, neopentane, nitrous oxide, 1,2,3-nonadecanetricarboxylic acid 2-hydroxytrimethyl ester, 1-nonene-3-yne, 1,4-pentadiene, n-pentane, perfluoropentane, 4-amino-0.4methylpentan-2-one, 1-pentene, 2-pentene, (cis and trans)-3-bromopent-1-ene, perfluoropent-1-ene, tetrachlorophthalic acid, 2,3,6-trimethyl-piperidine, propane, 1,1,1,2,2,3-hexafluoropropane, 1,2-epoxypropane, 2,2-difluoropropane, 2-aminopropane, 2-chloropropane, heptafluoro-1-nitropropane, heptafluoro-1-nitrosopropane, perfluoropropane, propene, hexafluoropropane, 1, 1,1,2,3,3-hexafluoro-2,3dichloropropane, 1-chloropropane, 1-chloropropylene, chloropropylene-(trans), chloropropane-(trans), 2-chloropropane, 2-chloropropylene, 3-fluoropropane, 3fluoropropylene, perfluoropropylene, perfluorotetrahydropyran, perfluoromethyltetrahydrofuran, perfluorobutylmethylether, perfluoromethylpentylether, propyne, 3,3,3-trifluoropropyne, 3-fluorostyrene, sulfur (di)-decafluoride (S₂F₁₀), sulfur hexafluoride, 2.4-diaminotoluene, trifluoroacetonitrile, trifluoromethyl peroxide, trifluoromethyl sulfide, tungsten hexafluoride, vinyl acetylene, vinyl ether, 1bromononafluorobutane, and perfluoroethers.

47. (New) The therapeutic composition according to claim 1, wherein the perfluorocarbon has between 4 and 10 atoms of fluorine.

Attorney Docket No.: IMARX1360-2

In re Application of: Evan C. Unger

Application No.: 10/622,027

Filed: July 16, 2003

Page 10 of 16

48. (New) The therapeutic composition according to claim 1, wherein the perfluorocarbon comprises a saturated, an unsaturated or a cyclic perfluorocarbon, selected from a group consisting of perfluoromethane, perfluoroethane, perfluoropropane, perfluorocyclopropane, perfluorobutane, perfluorocyclobutane, perfluoropentane, perfluorocyclopentane, perfluorobetane, perfluorocyclopentane, perfluorobetane, perfluorocyclopentane, perfluoro

- 49. (New) The therapeutic composition according to claim 48, wherein the perfluorocarbon is selected from a group consisting of perfluoropropane and perfluorobutane.
- 50. (New) The therapeutic composition according to claim 49, wherein the perfluorocarbon is perfluoropropane.
- 51. (New) The therapeutic composition according to claim 1, wherein the perfluoroether has between 4 and 10 atoms of fluorine.
- 52. (New) The therapeutic composition according to claim 1, wherein the gas precursor, if used, has between 4 and 8 atoms of carbon and between 12 and 15 atoms of fluorine.
- 53. (New) The therapeutic composition according to claim 52, wherein the gas precursor is selected from a group consisting of perfluoropentane, perfluorohexane, perfluorodecalin, perfluorotripropylamine, perfluoroctylbromide, perfluorobutylmethylether, perfluorotetrahydropyran, perfluoromethyltetrahydrofuran, and perfluoroether analogs containing between 4 and 6 carbon atoms, and optionally containing one halide ion.